Revolutionizing Gait Quality Monitoring in People with CIDP: An Instrumented Shoe Insole Solution

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Poster #005

BACKGROUND

- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a rare immune-mediated neurological disorder characterized by progressive limb weakness and sensory impairment[1]
- The ORBIT-CIDP, a non-interventional US-based trial is designed to elucidate the clinical characteristics of CIDP under real-world conditions, including disease progression, therapeutic efficacy, and patient reported outcomes to inform future research and support the development of evidence-informed models of care and therapeutic management **(Figure 1)**
- People with CIDP (PwCIDP) commonly experience gait dysfunction which negatively-impacts health-related quality of life. Its sensitivity to change makes gait a promising biomarker for disease control and/or progression[2]
- In response to the challenges of monitoring disease progression in PwCIDP[3], ORBIT-CIDP trial includes an exploratory objective to develop a digital biomarker that objectively quantifies gait quality on a standardized 0–100% scale
- Aligned with the real-world objectives of ORBIT-CIDP trial, this study assessed biomechanical gait in everyday environment in everyday environments using wearable instrumented shoe insoles as an alternative to in-clinic evaluations, reducing patient travel burden while enabling more frequent and ecologically valid assessments

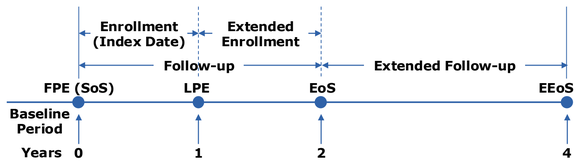
OBJECTIVE

- To develop a digital biomarker that passively assesses gait quality in PwCIDP using wearable instrumented shoe insoles

ORBIT-CIDP STUDY DESIGN AND ENDPOINTS

Figure 1. ORBIT-CIDP (Observational, Real-world, Digital Biomarker, and Integrated Treatment Outcomes in CIDP, NCT 06968975) Study Design

N~200
PwCIDP* (≥18 years age) actively receiving treatment** for ≥3 months who have residual disability (raw I-RODS score ≤44)



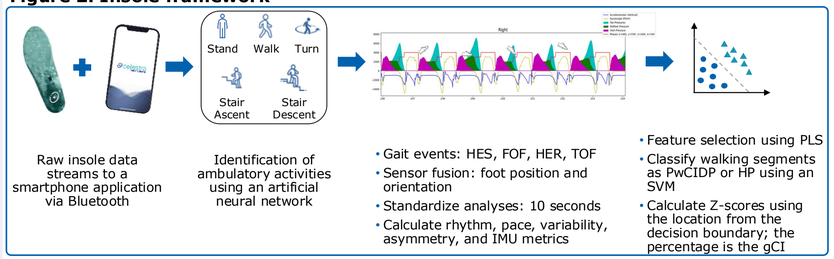
Primary Outcomes	Key Secondary Outcomes	Key Exploratory Outcomes
•I-RODS score at baseline, every three months over study duration and after treatment change •Annualized I-RODS response and relapse rates	•aINCAT score at baseline, every six months over study duration and after treatment change •Annualized aINCAT response and relapse rates	•Insole-recorded gait parameter at baseline, thrice a week over study duration and after treatment change •Correlation between insole-recorded gait parameters and clinical outcomes, I-RODS, aINCAT

*Criteria for exclusion: participation in any interventional clinical trial with an investigational drug at the time of enrollment, hyperreflexia in the medical record during a neurological exam the year before enrollment and after CIDP diagnosis; **Immunoglobulin G, mycophenolate mofetil, methotrexate, efgartigimod alpha, azathioprine, rituximab, cyclosporine. aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; EEoS, extended end of study, EoS, end of study; FPE, first participant enrollment; I-RODS, Inflammatory Rasch-Built Overall Disability Scale; LPE, last participant enrollment; PwCIDP, people with CIDP; SoS, start of study.

METHODS

- Fifty-seven PwCIDP (36 female, 21 male; mean age 59±11 years, height 170±10.5 cm, and mass 91±26 kg) were analyzed in the study
  - Baseline assessments showed mean(±SD) I-RODS scores of 31.7±7.6, lower limb INCAT of 1.71±1.07, and upper limb INCAT of 2.06±0.97
- Total 49 healthy participants (HP; 18 female, 31 male; mean age 36±13 years, height 174±9 cm, and mass 78±15 kg) were enrolled as controls
- All participants performed walking trials while wearing instrumented shoe insoles (Moticon, Germany) that streamed raw pressure, accelerometer, and gyroscope data to a smartphone app (Celestra Health Systems, Canada)
  - PwCIDP were asked to perform 10-minute free-living walks 3 times per week
  - HP performed a single 500-meter walking session (20 laps of 25 meters)
- Raw insole data were processed through insole framework **(Figure 2)** to produce 75 gait metrics
  - Independent t-tests identified significant differences between populations to be used for developing the gait composite index (gCI). Cohen's d quantified the magnitude of these differences, where d≥0.80 indicates a large effect size
- gCI scores were correlated to the PwCIDP's I-RODS and aINCAT scores at baseline using Spearman's Rho

Figure 2. Insole framework



FOF, foot on floor; gCI, gait composite index; HER, heel rise; HES, heel strike; HP, healthy participants; PLS, partial least squares; PwCIDP, people with CIDP; SVM, support vector machine; TOF, toe off.

RESULTS

- 121/144 (84%) of study participants opted in for smart insoles, and 73/121 (60.3%) participants performed at least one gait assessment
- Gait analysis across 75 metrics demonstrated remarkable sensitivity to CIDP-related functional impairment, with 93.3% of metrics showing significant differences between PwCIDP and HP. All pace, asymmetry, postural control, and rhythm metrics were significantly different.
- Effect sizes ranged from large to exceptional (d= 0.952–1.877), with stride velocity emerging as the most discriminating metric **(Table 1)**

Table 1. Most meaningful gait metrics across domains between PwCIDP and HP

Domain	Pace	Variability	Asymmetry	Postural Control	Rhythm
Number of Significant Gait Metrics	4	40	14	11	6
Most Meaningful Metrics (Effect Size*)	Stride Velocity (1.877)	Swing Time CV (1.627)	Swing Time Asymmetry (0.952)	Peak Euclidean Accelerometer (1.425)	Swing Percentage (1.288)

*Effect sizes interpreted as negligible (0-0.19), small (0.20-0.39), medium (0.40-0.79), and large (> 0.80). Pace: how quickly a person can move; Variability: stride-to-stride fluctuations; Asymmetry: percent difference between feet; Postural control: stability and balance; Rhythm: timing of gait cycles; Effect size: Cohen's d; $p<0.05$. CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CV, coefficient of variation; HP, healthy participants; LOESS, locally estimated scatterplot smoothing; PwCIDP, people with CIDP.

RESULTS (CONT…)

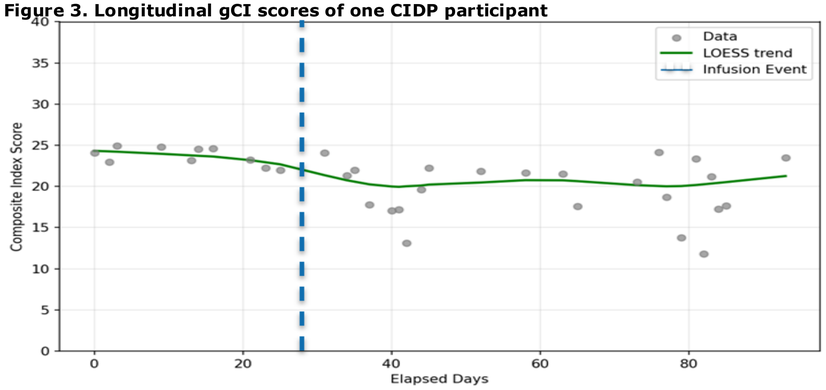
- The gCI had a moderate positive correlation with I-RODS (r=0.41, p=0.01) and combined INCAT (r=0.42, p=0.01), but not with INCAT Upper (r=0.23, p=0.20) **(Table 2)**
- Longitudinal gCI scores for a representative PwCIDP demonstrated a declining LOESS trend following the Ig infusion event **(Figure 3)**

Table 2. Correlation between gCI and clinical outcome measures

Outcome Measures	gCI	I-RODS	INCAT Lower	INCAT Upper	INCAT Combined
	r (p-value)				
gCI	1.00	0.41 (0.01)	0.42 (0.01)	0.23 (0.20)*	0.42 (0.01)
I-RODS	NA	1.00	0.59 (0.00)	0.41 (0.01)	0.60 (0.00)
INCAT Lower	NA	NA	1.00	0.37 (0.03)	0.85 (0.00)
INCAT Upper	NA	NA	NA	1.00	0.78 (0.00)
INCAT Combined	NA	NA	NA	NA	1.00

*Not significant. gCI, gait composite index; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-Built Overall Disability Scale; NA, not applicable; r, Spearman's Rho.

Figure 3. Longitudinal gCI scores of one CIDP participant



A LOESS curve is fit as the trendline. The participant noted an infusion event, marked by a dashed line, with a description of their "feet and legs feeling very heavy, upper back pain, legs feeling weak". CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; gCI, gait composite index; LOESS, locally estimated scatterplot smoothing.

CONCLUSIONS

- This study highlights the potential of instrumented shoe insoles as a passive, wearable solution for digitally evaluating gait quality in PwCIDP
- Direct-to-patient digital biomarkers enable patient-centered disease monitoring, enhancing engagement while capturing robust real-world natural history data
- These findings establish a foundation for next steps, including establishing minimal clinically important difference (MCID) thresholds and mapping gait signatures to clinical disease states (stable versus unstable)
- Full longitudinal analysis of the ORBIT natural history dataset will validate gait trajectories, support regulatory biomarker qualification, and position digital gait metrics as transformative, patient-centered endpoints for CIDP clinical trials and real-world disease management

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Disclosures

Karen M. Lynch, Alex Seluzhytsky: Employees of Sanofi; may hold stock or stock options. ***Karissa L. Gable:*** Consultant for Sanofi, Argenx, Immunovant, Takeda, InCircle, CSL Behring and Grifols. Service on the adjudication committee for clinical trials for Immunovant, Dianthus Argenx and Sanofi. Grant funding from the INC Base Registry Study. Honoraria payments for speaker presentations at AAN and AANEM. ***Matthew P. Mavor:*** may hold stock or stock options in Celestra Health Systems. ***Mohammad H. Akhavanfar, Kristen H.E. Beange:*** Employee of Celestra Health Systems; may hold stock or stock options. ***Ryan B. Graham:*** Scientific advisor for Celestra Health Systems; may hold stock or stock options. ***Jan C. Schuller:*** None.

Acknowledgments

The ORBIT-CIDP study is funded by Sanofi and conducted by PicnicHealth. Editorial support for this poster was provided by Hemali Savla, Ph.D. and Rachna Shukla, Ph.D. of Sanofi. We thank Alexandra Ilsley, PharmD, and Gerardo Gutierrez, PharmD of Sanofi for contributions to the planning, review, and coordination of this poster.

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Presented at the 78th American Academy of Neurology (AAN) Annual Meeting, April 18–22, 2026, Chicago, United States